

AMENDMENTS TO THE CLAIMS:

Please replace the claims with the claims provided in the listing below wherein status, amendments, additions and cancellations are indicated.

1. (Original) A method of deriving blood perfusion indices for a region of interest (ROI) of a subject, the method comprising the steps of:

administering a contrast agent to the subject during a dynamic imaging scan:

converting signal intensity data from raw images of the scan into contrast agent concentration data;

deriving parameters from the contrast agent concentration data using at least one transport function that accounts for delay and dispersion of the contrast agent; and

calculating the blood perfusion indices from the derived parameters.

2. (Original) A method according to claim 1 wherein the transport function represents a probability distribution function of transit times of the contrast agent through the subject.

3. (Original) A method according to claim 2 further comprising the step of using a first model to represent an arterial transport function $h_a(t)$ through a vessel leading to the ROI.

4. (Original) A method according to claim 3 further comprising using a second model to represent a tissue transport function $h_s(t)$ through the ROI.

5. (Original) A method according to claim 4 further comprising the step of selecting an arterial input function $AIF_a(t)$ in the vessel leading to the ROI by searching pixels taken of the contrast agent concentration data.

6. (Original) A method according to claim 5 further comprising the step of measuring the contrast agent concentration $C(t)$ remaining in the ROI.

7. (Original) A method according to claim 6 further comprising the step of representing $h_a(t)$ using a gamma-variate function (GVF) in the first model such that:

$$h_a(t) = \begin{cases} \frac{1}{A_1} (t - t_1)^{\alpha_1} e^{-(t-t_1)/\sigma_1} & (t \geq t_1) \\ 0 & (t < t_1) \end{cases}$$

where $A_1 = \sigma_1^{1+\alpha_1} \Gamma(1+\alpha_1)$, $\Gamma(\alpha) \equiv \int_0^\infty x^{\alpha-1} e^{-x} dx$ is the Gamma function, t_1 is the time taken for the contrast agent to move from the initial measurement of $AIF_a(t)$ to a vessel at the entry to the ROI, σ_1 and α_1 are related to the mean transit time and dispersion of $h_a(t)$.

8. (Original) A method according to claim 7 further comprising the step of estimating $h_a(t)$ after deriving values for parameters t_1 and σ_1 and setting $\alpha_1=0$ using the equation:

$$h_a(t) = \begin{cases} \frac{1}{\sigma_1} e^{-(t-t_1)/\sigma_1} & (t \geq t_1) \\ 0 & (t < t_1) \end{cases}$$

9. (Original) A method according to claim 8 further comprising the step of determining an estimate for the arterial input function $AIF_t(t)$ of the vessel at the entry to the ROI using the equation:

$$AIF_t(t) = AIF_a(t) \otimes h_a(t) \equiv \int_0^t AIF_a(\tau) h_a(t - \tau) d\tau$$

where \otimes is the convolution operator.

10. (Original) A method according to claim 9 further comprising the step of determining an estimate of blood flow F_t and an estimate of the tissue IRF $R_e(t)$ from the deconvolution of:

$$C(t) = (F_t / k_H) AIF_t(t) \otimes R_e(t)$$

where $k_H = (1 - H_a) / (1 - H_t)$ is a correction constant taking into account different values of arterial hematocrit H_a and tissue hematocrit H_t since the contrast agent remains in the extracellular fraction of blood (plasma).

11. (Original) A method according to claim 10 further comprising the step of determining an estimate for the tissue transport function $h_e(t)$ from the estimated $R_e(t)$ using the equation:

$$h_e(t) = - \frac{d}{dt} R_e(t)$$

12. (Original) A method according to claim 11 further comprising the step of determining a rise time and a mean transit time of $h_e(t)$ in order to determine parameters α_2 and σ_2 by assuming $t_2=0$, where t_2 , α_2 and σ_2 are parameters related to the mean transit time and dispersion of $h_e(t)$.

13. (Original) A method according to claim 11 further comprising the step of determining a peak height and a mean transit time of $h_e(t)$ in order to determine parameters σ_2 and t_2 by assuming $\alpha_2=0$, where t_2 , α_2 and σ_2 are parameters relating to mean transit time and dispersion of $h_e(t)$.

14. (Currently Amended) A method according to claim 12 ~~or claim 13~~ further comprising the step of representing a simulated transport function $h_s(t)$ using a GVF in the second model such that:

$$h_s(t) = \begin{cases} \frac{1}{A_2} (t - t_2)^{\alpha_2} e^{-(t-t_2)/\sigma_2} & (t \geq t_2) \\ 0 & (t < t_2) \end{cases}$$

where $A_2 = \sigma_2^{1+\alpha_2} \Gamma(1 + \alpha_2)$, t_2 , σ_2 and α_2 are parameters related to the mean transit time and dispersion of $h_s(t)$ through the ROI.

F-8566

15. (Original) A method according to claim 14 further comprising the step of estimating $h_s(t)$ using the derived values for parameters α_2 and σ_2 by setting $t_2=0$ using the equation:

$$h_s(t) = \frac{1}{A_2} t^{\alpha_2} e^{-t/\sigma_2} \quad (t \geq 0)$$

16. (Original) A method according to claim 14 further comprising the step of estimating $h_s(t)$ using the derived values for parameters σ_2 and t_2 by setting $\alpha_2=0$ using the equation:

$$h_s(t) = \begin{cases} \frac{1}{\sigma_2} e^{-(t-t_2)/\sigma_2} & (t \geq t_2) \\ 0 & (t < t_2) \end{cases}$$

17. (Currently Amended) A method according to claim 15 ~~or claim 16~~ further comprising the step of determining a simulated tissue IRF $R_s(t)$ using the equation:

$$R_s(t) = 1 - \int_0^t h_s(\tau) d\tau$$

18. (Original) A method according to claim 17 further comprising the step of determining a simulated contrast agent concentration $C_s(t)$ using the equation:

$$C_s(t) = (F_t/k_H) AIF_t(t) \otimes R_s(t)$$

19. (Original) A method according to claim 18 further comprising the step of fitting the simulated $C_s(t)$ to $C(t)$ using a least squares method according to:

F-8566

$$S = \sum_i (C(t) - C_s(t))^2$$

20. (Original) A method according to claim 19 further comprising the step of optimising the parameters F_t , t_1 , σ_1 , α_1 , σ_2 , α_2 and t_2 by minimizing S iteratively.
21. (Original) A method according to claim 20 further comprising the step of reducing the number of adjustable parameters by fixing $\alpha_1=0$ and $t_2=0$, or fixing $\alpha_1=0$ and $\alpha_2=0$ leading to five adjustable parameters.
22. (Currently Amended) A method according to claim 20 ~~or claim 21~~ comprising the step of further reducing the number of adjustable parameters by fixing a relative dispersion, $\beta_1=\sigma_1/(\sigma_1+t_1)$, of $h_a(t)$ resulting in σ_1 dependent on t_1 , ~~and therefore~~ leading to four adjustable parameters.
23. (Original) A method according to claim 22 further comprising the step of calculating quantitative blood perfusion indices from the optimized parameters of F_t , t_1 , σ_1 , α_1 , σ_2 , α_2 and t_2 .
24. (Original) A method according to claim 23 wherein the perfusion indices include any one or more of blood flow, blood volume, mean transit time, arterial delay time, arterial dispersion time or relative arterial dispersion, tissue dispersion time or relative tissue dispersion.

F-8566

25. (Original) A method according to claim 24 further comprising the step of repeating each previous step, apart from the step of selecting the AIF, on a pixel-by-pixel basis to produce quantitative maps of the perfusion indices for further analysis and presentation.
26. (Currently Amended) A method according to ~~any one of claims~~ claim 1 [[to 25]] wherein the ROI is a tissue.
27. (Currently Amended) A method according to ~~any one of claims~~ claim 1 [[to 25]] wherein the ROI is a pixel or a plurality of pixels in a tissue.
28. (Currently Amended) A method according to ~~any one of claims~~ claim 1 [[to 27]] wherein the scan is any one of CT, MRI or NM.
29. (Currently Amended) A method according to ~~any one of claims~~ claim 3 [[to 24]] wherein the vessel is an artery.
30. (Original) A method according to claim 29 further comprising determining a venous input function $VIF_a(t)$ from a draining vein to estimate an $AIF_a(t)$ where a selected artery has partial voluming, the vein being larger than the artery.
31. (Original) A method according to claim 30 further comprising the step of determining the profile of $VIF_a(t)$ from the draining vein.

32. (Original) A method according to claim 31 further comprising the step of scaling AIF_a(t) to have the same first-pass bolus peak area as the VIF_a(t) to minimize partial voluming effect from the AIF_a(t).

33. (Original) A method according to claim 32 wherein the first-pass bolus peak areas of the AIF_a(t) and VIF_a(t) profiles are obtained by fitting the profiles to gamma-variate function (GVF) profiles respectively to remove contrast recirculation effects.

34. (Currently Amended) A method according to ~~any one of claims~~ claim 17 [[to 33]] further comprising the step of determining a simulated tissue IRF R_s(t) in the case that the contrast agent does not always remain in the vascular system, such as in a tumour in the subject in order to determine blood perfusion indices and permeability indices using:

$$R_s(t) = 1 - \int_0^t h_s(\tau) d\tau + E e^{-kt} \int_0^t h_s(\tau) e^{k\tau} d\tau$$

where

$$h_s(t) = \begin{cases} \frac{1}{A_2} (t - t_2)^{\alpha_2} e^{-(t-t_2)/\sigma_2} & (t \geq t_2) \\ 0 & (t < t_2) \end{cases} ;$$

E is the extraction fraction of the tracer in the blood stream that leaks out of the vessel into tissue, and the tracer clearance rate constant $k = E \cdot F_t / V_e$ is a rate constant at which the leaked contrast agent diffuses back into the blood stream and leaves the tissue, V_e is volume fraction of the extravascular and extracellular space (EES).

35. (Original) A method according to claim 33 wherein a permeability surface area product PS is determined by $PS = -F_i \ln(1 - E)$.

36. (Currently Amended) Computer program means for deriving blood perfusion indices for a region of interest (ROI) of a subject by directing a processor to carry out ~~any of the method steps according to any one of claims~~ claim 1 [[to 35]] apart from the step of administering a contrast agent to the subject during a dynamic imaging scan.

37. (Original) Computer program means according to claim 36 further directing the processor to retrieve raw image data from the dynamic imaging scan of the subject after a contrast agent is administered to the subject.

38. (Original) A system of deriving blood perfusion indices for a region of interest (ROI) of a subject, the system comprising:

scanning means for providing a dynamic image scan of the subject during which a contrast agent is administered to the subject;

processor means linked to the scanning means for retrieving raw image data from the scan;

the processor means further:

converting signal intensity data included in the retrieved raw image data into contrast agent concentration data;

deriving parameters from the contrast agent concentration data using at least one transport function that accounts for delay and dispersion of the contrast agent; and

calculating the blood perfusion indices from the derived parameters.

39. (Original) A system according to claim 38 wherein the transport function represents a probability distribution function of transit times of the contrast agent through the subject.
40. (Original) A system according to claim 39 wherein a first model is used to represent an arterial transport function $h_a(t)$ through a vessel leading to the ROI.
41. (Original) A system according to claim 40 wherein a second model is used to represent a tissue transport function $h_s(t)$ through the ROI.
42. (Original) A system according to claim 41 wherein the processor means selects an arterial input function $AIF_a(t)$ in the vessel leading to the ROI by searching pixels taken of the contrast agent concentration data.
43. (Original) A system according to claim 42 wherein the processor means measures the contrast agent concentration $C(t)$ remaining in the ROI.